Remarks/Arguments

After entry of this Amendment, claims 25, 26, and 28-38, as amended, will be pending in the application for the Examiner's review and consideration. Claims 1-24 and 27 have been canceled without prejudice. The right to prosecute the subject matter of any of canceled claims 1-24 and 27 in this or in a continuation, continuation-in-part, or divisional application is hereby expressly reserved.

I. Claim Amendments

Claims 28-38 have been added. Claims 28, 29, 32, 33, 36, and 37 are supported, for example, by paragraph 27 on page 11 of the Specification as filed. Claims 30, 34, and 38 are supported, for example, by paragraph 41 on page 18 of the Specification as filed. Claim 31 is supported, for example, by paragraph 27 on pages 11 and 12 of the Specification as filed. Claim 35 is supported, for example, by paragraphs 31 and 32 on page 14 of the Specification as filed, which recite the optional inclusion of a non-toxic zinc salt and an amino acid in the composition. "If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims." M.P.E.P. § 2173.05(i). No new matter has been added to the claims by these amendments.

In addition, it is noted that the present claims are directed to the compositions recited in the method of treatment claims filed on November 13, 2009 in connection with co-pending U.S. Application Serial No. 12/015,258 ("'258 application"), assigned to Bioderm, Inc., which is also the assignee of the present application. Present claims 25, 26, and 28-30 recite the compositions of claims 9-12 of the '258 application; present claims 31-34 recite the compositions of claims 1-4 of the '258 application; and present claims 35-38 recite the compositions of claims 5-8 of the '258 application.

II. Declaration of Dr. Lorraine Faxon Meisner

Submitted herewith for the Office's consideration is a copy of the Declaration of Dr. Lorraine Faxon Meisner under 37 C.F.R. § 1.132 that was filed on April 9, 2009 in connection with the '258 application ("Meisner Declaration").

III. Rejections of Claims 25-27 under 35 U.S.C. § 103

Claims 25-27 stand rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 4,938,969 to Schinitsky and Meisner ("Schinitsky & Meisner") in view of U.S. Patent No. 5,804,594 to Murad ("Murad"); U.S. Patent No. 5,902,591 to Herstein ("Herstein") or U.S. Patent No. 5,140,043 to Darr and Pinnell ("Darr"); THE MERCK INDEX, entry 855 (9th ed. 1976) ("Merck Index"); and J.P. Yuan & F. Chen, *J. Agric. Food Chem.*, 46: 5078-82 (1998) ("Yuan"). These rejections have been rendered moot as to claim 27 by its cancellation without prejudice. As to claims 25-26, these rejections are respectfully traversed for the reasons discussed below.

Claims 25-26 and new claims 28-30 recite topical compositions comprising: at least 10% (w/v) ascorbic acid; approximately 10% to 25% (w/v) glucosamine; and water, wherein the composition has a pH of about 3.5 to about 4.1; and wherein the composition is prepared by a process comprising: (a) dissolving about 10% to about 50% of the ascorbic acid in water at a temperature of between about 60°C to about 90°C to provide an aqueous ascorbic acid solution of at least 20% (w/v); (b) cooling the aqueous ascorbic acid solution to below about 40°C; (c) combining the aqueous ascorbic acid solution with water, glucosamine, and ascorbic acid to provide a composition comprising water, approximately 10% to 25% (w/v) glucosamine and at least 10% (w/v) ascorbic acid; and (d) adjusting the pH of the composition to about 3.5 to about 4.1.

The primary reference Schinitsky & Meisner fails to disclose or provide any guidance as to each and every recitation of claims 25-26 and 28-30

Schinitsky & Meisner refers to a composition for topical application to reduce epidermal wrinkling resulting from intrinsic aging or photo-aging, which comprises from about 2 to about 20% ascorbic acid, about 1 to about 10% tyrosine, and about 0.5 to about 5% zinc sulfate in a pharmaceutically acceptable vehicle. (Schinitsky & Meisner, col. 2, ll. 38-53).

Schinitsky & Meisner fails to disclose or provide any guidance as to a composition that has glucosamine.

Further, Schinitsky & Meisner fails to disclose or provide any guidance as to a composition that has a pH of about 3.5 to about 4.1. In fact, Schinitsky & Meisner is completely silent as to pH.

Further still, Schinitsky & Meisner fails to disclose or provide any guidance as to a composition comprising ascorbic acid that has been prepared by the process recited in the claims. Again, Schinitsky & Meisner is completely silent as to the process used to prepare the compositions.

The secondary references cited by the Office fail to remedy the deficiencies of the primary reference Schinitsky & Meisner as to claims 25-26 and 28-30

The Office cites Murad, Herstein or Darr, Merck Index, and Yuan in order to remedy the above-described deficiencies of Schinitsky & Meisner. This, however, is unavailing for the reasons discussed below.

Murad refers to compositions having: (i) a sugar compound that is converted to glycosaminoglycans in the human bloodstream; (ii) a primary antioxidant (*e.g.*, ascorbic acid); (iii) at least one amino acid to assist in thickening the skin; (iv) and one or more transition metal compounds (*e.g.*, copper, zinc, or manganese compounds) in an amount effective to bind collagen and elastic tissue to rebuild the skin. (Murad, col. 5, l. 6 to col. 7, l. 12).

Murad fails to disclose or provide any guidance as to a composition that has a pH of about 3.5 to about 4.1. Like Schinitsky & Meisner, Murad is completely silent as to pH.

Further, Murad fails to disclose or provide any guidance as to a composition comprising ascorbic acid that has been prepared by the process recited in the claims. Murad simply states that the compositions may be prepared by "any of the methods of pharmacy." (Murad, col. 9, ll. 34-49).

"pH of about 3.5 to about 4.1"

The Office cites Herstein or Darr to provide the missing teaching of a pH of about 3.5 to about 4.1.

Herstein refers to stable topical emulsions for cosmetic/pharmaceutical purposes comprising a powdered ascorbic acid phase and a liquid phase, the liquid phase containing an emulsion stabilizingly effective amount of an organoclay material. (Herstein, abstract). The Office states that Herstein "teaches that a pH within 3.5 to 4.1 is preferred to facilitate entry of ascorbic acid into the skin and stabilize the ascorbic acid molecule." (Office Action, p. 3). Herstein, however, also teaches that the organoclay ingredient is essential for stability of the emulsion: "As can be seen from the data, the physical appearance of the emulsion initially is

acceptable and remains acceptable (no breaking of the emulsion) after 25 days. Without the organoclay ingredient, the emulsion would begin to break down after a few days, i.e., 2-3 days." (Herstein, col. 13, ll. 35-41). By disclosing that the emulsions having a pH within the range of 3.5 to 4.1 are unstable if they lack an organoclay ingredient, Herstein would certainly not guide the person of ordinary skill in the art to incorporate the pH of Herstein into the compositions of Schinitsky & Meisner or Murad, which do not contain an organoclay ingredient, as suggested by the Office.

Darr refers to a stable topical composition which consists essentially of at least about 1 wt. % ascorbic acid in water and a carrier for topical application, where the pH of the composition is no more than about 3 to 3.5, and preferably no more than about 2.5. (Darr, col. 3, ll. 18-32). Despite Darr's emphasis on compositions having pH below 3.5, the Office selects and relies upon Dar's Examples III and IV to provide a teaching that at a pH of 4.5 or 4.2, a 5% ascorbic acid solution remains stable. (Office Action, p. 5). It is respectfully submitted, however, that Dar's Examples III and IV describe experiments where ascorbic acid compositions were stored for 6 to 12 weeks in the dark, at low temperature (4°C), in capped microfuge tubes. Thus, Darr does not disclose ascorbic acid compositions above pH 3.5 that are stable under standard storage conditions. Accordingly, Darr would not guide the person of ordinary skill in the art to formulate an ascorbic acid composition having a pH of about 3.5 to about 4.1 in order to arrive at a topical composition as recited in the claims.

Moreover, as discussed in the Meisner Declaration submitted herewith, at the time of the invention, it would have been entirely unexpected that an ascorbic acid composition would be stable enough for use in a topical composition at a pH of about 3.5 to about 4.1. (Meisner Declaration, ¶¶ 11-12). Dr. Meisner's conclusion is supported not only by the Bauernfeind, Hajratwala, and Kassem articles cited in her Declaration, but also by Herstein and Darr as described above, which were cited by the Office.

For these reasons, neither Herstein nor Darr, when combined with the teachings of Schinitsky & Meisner and Murad, discloses or provides any guidance as to the recited compositions having a pH of about 3.5 to about 4.1.

"(a) dissolving about 10% to about 50% of the ascorbic acid in water at a temperature of between about 60°C to about 90°C to provide an aqueous ascorbic acid solution of at least 20% (w/v); (b) cooling the aqueous ascorbic acid solution to below about 40°C"

The Office cites Merck Index and Yuan to provide the missing teaching of the steps of "(a) dissolving about 10% to about 50% of the ascorbic acid in water at a temperature of between about 60°C to about 90°C to provide an aqueous ascorbic acid solution of at least 20% (w/v)" and "(b) cooling the aqueous ascorbic acid solution to below about 40°C."

Merck Index refers to the compound ascorbic acid and states that the solubility of ascorbic acid in hot water is "80% at 100°; 40% at 45°." Merck Index does not disclose or provide any guidance as to a topical composition comprising ascorbic acid, or as to a method for preparing such a topical composition that includes steps (a) and (b) above. At most, Merck Index teaches the person of ordinary skill in the art that ascorbic acid has a particular solubility in water at 100°C and 45°C.

Yuan refers to experiments in which solutions of ascorbic acid in aqueous media at pH 4 were heated at 60°C or 100°C for 2 hours. (Yuan, p. 5079 and Figure 1). Yuan reports the presence of at least three degradation products of ascorbic acid in each solution after heating: furfural; 3-hydroxy-2-pyrone; 2-furoic acid (only in the solution heated at 100°C); and an unknown compound. (Yuan, p. 5081-82). Yuan does not disclose or provide any guidance as to a topical composition comprising ascorbic acid, or as to a method for preparing such a topical composition that includes steps (a) and (b) above. To the contrary, Yuan teaches away from heating ascorbic acid at a temperature of between about 60°C to about 90°C, as recited in the claims, by showing that heating ascorbic acid at 60°C or 100°C causes the ascorbic acid to degrade. The person of ordinary skill in the art would recognize that it is not desirable to have degradation products in a topical composition, such as that recited in the present claims.

Therefore, neither Merck Index nor Yuan, when combined with the teachings of Schinitsky & Meisner, Murad, Herstein and/or Darr, discloses or provides any guidance as to topical compositions of ascorbic acid made by a process including steps (a) and (b) above, as recited in the claims.

For these reasons, the Office has failed to make out a *prima facie* case of obviousness of claims. Accordingly, the rejections of claims 25-27 under 35 U.S.C. § 103 as obvious over Schinitsky & Meisner in view of Murad, Herstein or Darr, Merck Index, and Yuan cannot stand and should be withdrawn.

IV. Arguments in Support of Patentability of New Claims 31-34

Claims 31-34 recite topical compositions consisting essentially of: at least 10% (w/v) ascorbic acid; approximately 10% to 25% (w/v) glucosamine; and water, wherein the composition has a pH of about 3.5 to about 4.1. The term "consisting essentially of" in claims 31-34 limits the scope of claims 31-34 to the recited ingredients and those that do not materially affect the basic and novel characteristic(s) of claimed method, in accordance with M.P.E.P. § 2111.03. In particular, as discussed below, it is submitted that the term "consisting essentially of" in claims 31-34 serves to exclude an amino acid and a transition metal compound.

It is noted that the Office questioned this claim construction in connection with claims 1-4 of the'258 application in the Advisory Action mailed on October 15, 2009. The Office stated:

> The Examiner acknowledges the explanation of the "consisting essentially of" phrase as requested in the interview (7/31/2009). However, the Applicant's argument that the phrase "consisting essentially of" excludes both amino acids and transition metal does not provide evidence that the inclusion of the same would materially affect the basic and novel characteristics of the claimed invention. Applicant's own specification indicates that non-toxic zinc salts and sulfur containing amino acids are suitable for use in the claimed invention, i.e. would have the same basic and novel characteristics of treating rosacea or acne.

(Advisory Action mailed on October 15, 2009 for the '258 application, continuation sheet, #11, citing *In re Herz*, 537 F.2d 549 (C.C.P.A. 1976)).

In order to advance prosecution of the present application, we address the concerns expressed in the Advisory Action for the '258 application here. It is believed that the amino acid and transition metal compound materially affect the basic and novel characteristic(s) of the claimed compositions because they are active ingredients that, if present, would supplement the activity of the claimed compositions when topically applied to a patient. The person of ordinary skill in the art would have recognized these components as active ingredients by recourse, for

example, to the Murad reference cited by the Office and discussed below. Murad states that amino acids are effective, for example, to assist in thickening the skin and that transition metal compounds are effective, for example, to bind collagen tissue to rebuild the skin. (Murad, col. 5, l. 6 to col. 7, l. 12). The present facts differ substantially from those presented in *Herz*, which dealt with the inclusion of a well-known excipient (dispersant), and not an active ingredient.

The primary reference Schinitsky & Meisner fails to disclose or provide any guidance as to each and every recitation of claims 31-34

As discussed above, Schinitsky & Meisner fails to disclose or provide any guidance as to a composition that contains glucosamine.

Further, Schinitsky & Meisner fails to disclose or provide any guidance as to a composition that has a pH of about 3.5 to about 4.1. In fact, Schinitsky & Meisner is completely silent as to pH.

Further still, Schinitsky & Meisner fails to disclose or provide any guidance as to a composition that does not comprise the amino acid tyrosine. To the contrary, every composition referred to in Schinitsky & Meisner contains tyrosine as an ingredient.

The secondary references cited by the Office fail to remedy the deficiencies of the primary reference Schinitsky & Meisner as to claims 31-34

The Office cites Murad, Herstein or Darr, Merck Index and Yuan in order to remedy the above-described deficiencies of Schinitsky & Meisner. This, however, is unavailing for the reasons discussed below.

As discussed above, Murad refers to compositions having, *inter alia*, an amino acid and a transition metal compound. Murad does not provide any guidance for the person of ordinary skill in the art to choose to remove the amino acid and transition metal compound (e.g., non-toxic zinc salt) from the Murad compositions. Rather, Murad stresses the importance of the amino acid and transition metal compound by stating that these ingredients are effective to thicken the skin, and to bind collagen and elastic tissue to rebuild the skin, respectively. Further, Murad fails to disclose or provide any guidance as to a composition that has a pH of about 3.5 to about 4.1. Like Schinitsky & Meisner, Murad is completely silent as to pH.

The Office cites Herstein or Darr to provide the missing teaching of a pH of about 3.5 to about 4.1. This is unavailing for substantially the same reasons as discussed above for claims 25-26 and 28-30.

Merck Index and Yuan fail to remedy the deficiencies of Schinitsky & Meisner, Murad, and Herstein or Darr because, as discussed above, they too fail to disclose or provide any guidance as to a composition that: (a) contains ascorbic acid, glucosamine, and water; (b) has a pH of about 3.5 to about 4.1; or (c) does not comprise an amino acid or a non-toxic zinc salt.

For these reasons, it is believed that claims 31-34 are patentable over the cited references, and are in condition for allowance.

V. Arguments in Support of Patentability of New Claims 35-38

Claims 35-38 recite compositions comprising: at least 10% (w/v) ascorbic acid; approximately 10% to 25% (w/v) glucosamine; and water, wherein: the composition has a pH of about 3.5 to about 4.1; the composition does not comprise an amino acid; and the composition does not comprise a non-toxic zinc salt.

It is respectfully submitted that claims 35-38 are novel and non-obvious over & Meisner in view of Murad, Herstein or Darr, Merck Index, and Yuan for substantially the same reasons as described for claims 31-34 above. Claims 35-38 recite compositions that comprise ascorbic acid, glucosamine, and water, and do not comprise an amino acid or a non-toxic zinc salt. Claims 31-34 likewise exclude an amino acid and a non-toxic zinc salt by virtue of the claim term "consisting essentially of." Claims 35-38, therefore, differ from the disclosures of the cited references for substantially the same reasons as do claims 31-34.

Accordingly, it is believed that claims 35-38 are patentable over the cited references, and are in condition for allowance.

VI. Conclusion

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims are in condition for allowance. Early and favorable action by the Examiner is earnestly solicited. If any outstanding issues remain, the Examiner is invited to contact the undersigned at (212) 497-7731 to discuss the same before issuing a further Action.

No fee is believed to be due for the submission of this response. Should any fees be required, please charge all such fees to Wilson, Sonsini, Goodrich & Rosati Deposit Account No. 23-2415 (36091-701.501).

Respectfully submitted,

Dated: December 3, 2009

By: /Gina R. Gencarelli/
Gina R. Gencarelli
Reg. No. 59,729

WILSON, SONSINI, GOODRICH & ROSATI PC
650 Page Mill Road
Palo Alto, CA 94304
Phone: (650) 493-9300
Fax: (650) 493-6811
Customer No. 21971